

Appendix 4.1

Genotypic and Phenotypic Analyses of Influenza Viruses Shed by Recipients of Cold Adapted, Live Attenuated Influenza Virus Vaccine

Table 1: Nucleotide Changes in Attenuating Genes of Viruses Shed after Vaccine Administration

Table 2: Clustering of Nucleotide Changes in Attenuating Genes of Viruses Shed after Vaccine Administration

Table 1. Nucleotide Changes in Attenuating Genes of Viruses Shed after Vaccine Administration

H1N1							
Isolate #	PB2	PB1	PA	NP	M	NS	Total Changes Amino Acid /Nucleotide
1	+			+			2/2
2	+	+			+		3/3
3				+			1/1
4			+	+			0/2
5		+					1/1
6	+	+	+	+	+		3/7
7			+		+		1/2
8				+			1/1
9	+			+	+		4/4
10	+			+			2/2
11	+						0/1
12		+					0/1
13	+			+			2/2
14		+					0/2
15	+			+			2/2
16	+			+			2/2
17							0/0
18							0/0
19							0/0
20							0/0
21							0/0
							24/35
Total	9/21	5/21	3/21	10/21	4/21	0/21	

* = Encoding for two proteins

+= Nucleotide change

a, b = Multiple isolates from same participant

Table 1. (cont) Nucleotide Changes in Attenuating Genes of Viruses Shed after Vaccine Administration

H3N2							
Isolate #	PB2	PB1	PA	NP	M	NS	Total Changes Amino Acid /Nucleotide
1				+	+		2/2
2		+	+	+			2/3
3				+			1/1
4		+		+	+		3/3
5				+			1/1
6	+			+	+		3/4
7		+	+	+	+		3/6
8				+	+		1/2
9	+	+					1/2
10	+	+		+			3/6
11	+	+		+	+		3/5
12							0/0
							23/35
Total	4/12	6/12	4/12	9/12	6/12	0/12	

* = Encoding for two proteins

+= Nucleotide change

a, b = Multiple isolates from same participant

Table 1. (cont) Nucleotide Changes in Attenuating Genes of Viruses Shed after Vaccine Administration

B Isolate #	PB2	PB1	PA	NP	M	NS	Total Changes Amino Acid /Nucleotide
1			+				0/1
2		+			+		0/2
3				+			1/1
4				+			1/1
5				+	+		3*/2
6				+	+		3*/2
7	+				+		1/2
8					+		1/1
9			+				0/1
10		+					1/1
11					+		1/1
12			+				1/1
13							0/0
14							0/0
15					+		1/1
16					+		1/1
17							0/0
18							0/0
19							0/0
20							0/0
21							0/0
22							0/0
							15/18
Total	1/22	2/22	3/22	0/22	10/22	2/22	

* = Encoding for two proteins

+= Nucleotide change

a, b = Multiple isolates from same participant

Table 2. Clustering of Nucleotide Changes in Attenuating Genes of Viruses Shed after Vaccine Administration

	H1N1	H3N2	B
PB2	A B C C C C C C	D E E E F	G
PB1	H I I J J K L	M N K K K O	P Q
PA	R S S	T U V W X	Y Z AA
NP	BB CC CC DD EE FF FF FF FF FF FF	BB CC CC CC CC CC CC GG HH EE FF	
M	II JJ KK LL	MM MM MM MM NN OO	PP PP PP PP PP PP QQ
NS			RR RR